Remarks

I. Status of the Claims

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-11, 13, 17, 28, 36-41, 46, and 49-65 are pending in the application, with claim 1 being the independent claim.

II. The Amendments

Paragraph [0160] of the specification has been amended to correctly recite the unabbreviated chemical names of DOSPA, DORI ester, DORIE diether, DORI ester/ether, and DC-Chol. One of ordinary skill in the art would know the unabbreviated chemical names of DOSPA, DORI ester, DORIE diether, DORI ester/ether, and DC-Chol at the time the application was filed. For instance, U.S. Pat. No. 5,264,618 (Exhibit A) at cols. 9 and 10 discloses the unabbreviated chemical names of DORI ester, DORIE diether, and DORI ester/ether. Wheeler, C.J. *et al., PNAS 93*:114545-11459 (1996) (Exhibit B) at page 11454 (abbreviations section) discloses the unabbreviated chemical name of DOSPA. The abstract of Zuidam N.J. *et al., Biochim. Biophys. Acta. 1329*:211-222 (1997) (Exhibit C) discloses the unabbreviated chemical name of DC-Chol.

Paragraph [0161] of the specification has been amended to correctly recite the unabbreviated chemicals names of DLYS-DABA-GLY-DORI diester and DLYS-DABA-DORI diester. One of ordinary skill in the art would know the unabbreviated chemical names of DLYS-DABA-GLY-DORI diester and DLYS-DABA-DORI diester and that the "□" in paragraph [0161] should be replaced with "β" at the time the application was filed. For instance, U.S. Pat. No. 5,264,618 (Exhibit A) at col. 10 discloses that DLYS-DABA-DORI diesters are lysine containing adducts of DORI,

having lysine groups attached at the hydroxyl group of the β-hydroxyethyl moiety through a diaminobenzoic acid linker.

Claim 1 has been amended to indicate that both the antibody and the fragment thereof are specific for a cell surface marker. Support for this amendment can be found in claim 1 as originally filed and at page 19, paragraph [0054] of the specification. Claim 1 has also been amended to recite "wherein said CD1d complex comprises a CD1d molecule or fragment thereof and a β2-microglobulin molecule or fragment thereof." Support for this amendment can be found at page 11, paragraph [0026]. Finally, strictly for clarity, claim 1 was amended to recite "a CD1d complex." Applicants submit that claim 1 recites "comprising" and, therefore, the phrase "one or more" is redundant.

Claim 2 has been amended for clarity and recites "said CD1d molecule."

Claim 8 has been amended to recite "wherein said antibody fragment is a scFv fragment." Support for this amendment can also be found at page 19, paragraph [0054] of the specification.

Claim 40 has been amended to recite "wherein the CD1d complex is linked in a fusion protein with the antibody or fragment thereof." Support for this amendment can be found in claim 40 as original filed and at page 8, paragraph [0014]; page 13, paragraph [0033]; page 14, paragraph [0034]; and page 70, paragraph [0210] of the specification.

Claims 7-9 have been amended to depend solely from claim 1. Claims 13, 17, 28, 36-41, and 46 have been amended to correct improper multiple dependencies. Claims 1 and 7- 9 have also been amended to correct minor informalities.

Claims 12, 14-16, 18-27, 29-35, 42-45, 47, and 48 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein.

New claims 49-65 are sought to be added. Support for new claim 49 can be found in claim 11 as originally filed. Support for new claim 50 can be found in Examples 4, 10, and 13 of the specification. Support for new claim 51 can be found in Example 13 of the specification. Support for new claims 52 and 53 can be found at page 20, paragraph [0056] of the specification. Support for new claims 54-56 can be found at page13, paragraph [0030] of the specification. Support for new claims 57-59 can be found at page 14, paragraph [0033] of the specification. Support for new claims 60-62 can be found at page 12, paragraph [0030] of the specification. Support for new claims 63-65 and page 13, paragraph [0030] of the specification.

Accordingly, no new matter is believed to have been added by these amendments and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

III. Objection to the Benefit Claim

At page 3 of the Office Action dated August 31, 2009, the Examiner states that "the filing date of the instant claims 1-4, 8, 10, 11 and 40 is deemed to be the filing date of PCT/US03/30238" because the priority application EP Appl. No. 02405838.0 "does not support the claimed limitations of the instant application." Specifically, the Examiner states that the priority application "does not provide support for a compound comprising greater than one CD1d complex, nor for an antibody with specificity for

Her2/neu or the other cell surface markers recited in instant claim 11." Applicants respectfully disagree with the Examiner's assertion.

Strictly for clarity, claim 1 was amended to recite "a CD1d complex." Nonetheless, Applicants submit that the priority application does in fact teach compounds comprising greater than one CD1d complex at page 4, lines 13-14 and antibodies with specificity for CEA, Her2/neu, and CD20 at page 1, line 19. One of ordinary skill in the art would know that Her2/neu is also known as ErbB-2 at the time the application was filed. *See* Hudziak, R.M. *et al., PNAS 85*:5102-5106 (1988) (Exhibit D). As such, the priority application provides support for the elected species. The application also generally discloses the use of monoclonal antibodies specific for tumor-associated antigens (TAAs) at page 1, lines 12-13 and at page 6, lines 31-34. One of ordinary skill in the art would appreciate that EGFR type I and type II, CD19, CD22, Muc-1, PSMA and STEAP are all TAAs.

As the priority application adequately supports both the elected species and the pending claims, Applicants respectfully request the benefit of the September 27, 2002 priority date and the withdrawal of the above objection.

IV. Rejections

A. Rejections under 35 U.S.C. § 112

Claims 1-4, 8, 10, 11, and 40 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants respectfully traverse this rejection.

The Examiner asserts that claim 1 does not clearly specify whether both the antibody and the fragment thereof are specific for a cell surface marker. Applicants have

amended claim 1 to indicate that both the antibody and the fragment thereof are specific for a cell surface marker as described above.

The Examiner asserts that with respect to claim 8, it is unclear "how an intact antibody can be a fragment of an antibody." (Office Action at page 3). Applicants submit that the specification at page 19, paragraph [0054] clearly states that an "antibody" includes intact molecules as well as antibody portions (such as, for example, Fab and F(ab')2 portions and Fv fragments) which are capable of specifically binding to a cell surface marker. As such, Applicants respectfully submit that claim 8 is definite.

However, without acquiescing in the propriety of the rejection, and solely in the interest of expediting prosecution, Applicants have amended claim 8 to recite "wherein said antibody fragment is a scFv."

The Examiner asserts that base claims 1 and 2 recite "one or more CD1d molecules," but claim 40 lacks a reference to just one CD1d molecule. Applicants have amended claims 1 and 2 to recite "a CD1d complex" and "said CD1d molecule," respectively.

In view of the above, it is respectfully requested that the rejections of claims 1-4, 8, 10, 11, and 40 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

B. Rejections under 35 U.S.C. § 103

1. First 35 U.S.C. § 103(a) Rejection

Claims 1-4, 10, 11, and 40 are rejected under 35 U.S.C. § 103(a), as allegedly obvious over Donda *et al.* (*Canc. Immun. 3*:11 (2003)) in view of U.S. Publ. No.

2002/0071842 A1 and Fuji *et al.* (*Nat. Immunol. 3*:867-875 (2002)). Applicants respectfully traverse this rejection.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki,* 745 F.2d 1468, 1471-73 (Fed. Cir. 1984). In view of *KSR Int'l. Co. v. Teleflex Inc.,* 550 USPQ2d 1385 (2007), the Office has published Examination Guidelines to aid Examiners in formulating obviousness rejections. See MPEP § 2141-2143 (hereinafter "the Examination Guidelines"). Seven rationales are suggested by which obviousness may be found, *e.g.,* by combining elements in the art or substituting one known element for another. As a common thread through all the rationales, the Examiner must establish on the record that a person of ordinary skill in the art would have recognized that the results of the combination or substitution were predictable.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness.

a. Donda et al.

As discussed above, Applicants submit that the present application is entitled to the priority date of September 27, 2002. Donda *et al.,* the primary reference, was not published until August 14, 2003 and, therefore, is not a proper reference for an obviousness rejection.

b. U.S. Publ. No. 2002/0071842 A1

As discussed during Applicants' Preliminary Amendment and Reply to Requirement for Unity of Invention and Election of Species filed February 23, 2009, Applicants submit that U.S. Publ. No. 2002/0071842 A1 does not teach CD1d/β2-microglobulin-antibody compounds of the present invention that specifically target cells

expressing cell surface markers. Rather, this reference merely discusses CD1d fusion polypeptides used to screen and identify CD1-restricted T cells and novel CD1 antigens.

c. Fuji et al.

While Fuji *et al.* mentions a preference for administering α-GalCer pulsed dendritic cells over free α-GalCer to adult mice, Fuji *et al.* also does not teach CD1d/β2-microglobulin-antibody compounds of the present invention that specifically target cells expressing cell surface markers. Accordingly, Fuji *et al.* does not cure the deficiencies of U.S. Publ. No. 2002/0071842 A1.

Without Donda *et al.,* the primary reference, the combination of U.S. Publ. No. 2002/0071842 A1 and Fuji *et al.* fails to recite all the claim elements. Additionally, the missing claim elements are not of common knowledge.

Thus, a person of ordinary skill in the art would not predictably arrive at the claimed invention even if that person were to combine U.S. Publ. No. 2002/0071842 A1 and Fuji *et al.* Therefore, a *prima facie* case of obviousness has not been established.

Accordingly, it is respectfully requested that the rejection of claims 1-4, 10, 11, and 40 under 35 U.S.C. § 103(a), as allegedly obvious, be reconsidered and withdrawn.

2. Second 35 U.S.C. § 103(a) Rejection

Claim 8 is rejected under 35 U.S.C. § 103(a), as allegedly obvious over Donda *et al.* (*Canc. Immun. 3*:11 (2003)) in view of U.S. Publ. No. 2002/0071842 A1 and Fuji *et al.* (*Nat. Immunol. 3*:867-875 (2002)) as applied to claims 1-4, 10, 11, and 40, and further in view of Pavlinkova *et al.* (*Canc. Immunol. Immunotherap. 49*:267-275 (2000)). Applicants respectfully traverse this rejection.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness. As discussed above, Applicants submit that Donda *et al.* is not a proper

reference as it was published after the Applicants' priority application and the combination of U.S. Publ. No. 2002/0071842 A1 and Fuji *et al.* would not allow a skilled person to predictably arrive at the claimed invention.

While Pavlinkova *et al.* discusses some advantages of scFv molecules, such as their "excellent penetration into tumor tissue, rapid clearance rate, and much lower exposure to normal organs," Pavlinkova *et al.* also does not teach CD1d/β2-microglobulin-antibody compounds of the present invention that specifically target cells expressing cell surface markers. Accordingly, Pavlinkova *et al.* does not cure the deficiencies of U.S. Publ. No. 2002/0071842 A1 combined with Fuji *et al.*

Without Donda *et al.,* the primary reference, the combination of U.S. Publ. No. 2002/0071842 A1, Fuji *et al.,* and Pavlinkova *et al.* fails to recite all the claim elements. Additionally, the missing claim elements are not of common knowledge.

Thus, a person of ordinary skill in the art would not predictably arrive at the claimed invention even if that person were to combine U.S. Publ. No. 2002/0071842 A1, Fuji *et al.* and Pavlinkova *et al.* Therefore, a *prima facie* case of obviousness has not been established.

Accordingly, it is respectfully requested that the rejection of claim 8 under 35 U.S.C. § 103(a), as allegedly obvious, be reconsidered and withdrawn.

C. Obvious-Type Double-Patenting

Claims 1-4, 8, 10, 11, and 40 are rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claim 78 of co-pending U.S. Appl. No. 12/034,737. Applicants respectfully traverse this rejection.

As discussed above, the present application claims the benefit of the September 27, 2002 priority date. Co-pending U.S. Appl. No. 12/034,737 was filed on February 21, 2008. Therefore, the present application is the earlier-filed application.

Further, Applicants wish to direct the Examiner's attention to M.P.E.P. § 804, which recites:

> If a "provisional" nonstatutory obviousness-type double-patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer.

Claim 78 in co-pending U.S. Appl. No. 12/034,737 has yet to be examined. Applicants believe that the claims of the present application are now in condition for allowance, with the ODP rejection as the last remaining rejection. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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